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Chapter 1

Screening for Colorectal Cancer

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/57506

1. Introduction

It has become an acknowledged fact that Colorectal Cancer (CRC) is a worldwide problem, with an annual incidence of approximately 1 million cases and an annual mortality of more than 500,000. Furthermore, the absolute number of cases will increase over the next two decades as a result of the aging and expansion of populations in both the developed and developing countries.

Apparently, CRC is the second most common cause of cancer related mortality among men and women in the world; so, most CRCs arise from sporadic adenomas, and a few from genetic polyposis syndromes or inflammatory bowel disease (IBD). The term "polyp" refers to a discrete mass that protrudes into the intestinal lumen. Therefore, the reported prevalence of adenomatous polyps, on the basis of screening colonoscopy data, is in the range of 18–36%.

The fact is that the risk for CRC varies from country to country and even within countries; the risk also varies among individual people based on diet, lifestyle, and hereditary factors. The most common neoplastic outcome of colorectal cancer screening is the adenoma. After having removed, patients need to be placed in a follow-up surveillance programme, very much similar to the patients with identified and treated cancer.

In the western world, we are very much aware that colorectal cancer has become an important health problem as each year, over 380,000 persons are diagnosed with colorectal cancer; bout half of these, patients die of the disease making colorectal cancer the second leading cause of cancer deaths in Europe. An estimated figure reveals that almost one million people suffering from colorectal cancer are going through cost – intensive treatments putting a huge burden on the healthcare system.

Screening is defined as population based testing in an asymptomatic individual to identify particular disease. The aim of screening is to lower the burden of cancer in the population by

discovering latent disease in its early stages and treating it more effectively than diagnosed later when symptoms have appeared. As such, screening is a commendable method to reduce the burden of the disease. However, population screening targets a predominantly healthy population, and should therefore only be conducted after a careful consideration of both harms and benefits.

In 1968 the World Health Organization [1] (WHO) defined the first set of principles of population screening (Wilson &Junger 1968). These principles are still valid today.

The desirable features for community screening program for any disease are:

1. The disease should be an important health problem
2. Natural history of the disease must be known
3. The disease should be detectable at an early stage
4. Benefits of early detection should be there
5. Simple test should be available at early stage
6. The test should have high sensitivity and specificity and should be safe, effective, acceptable, inexpensive, and repeatable after an interval
7. Services should be in place to treat the early disease
8. Benefits of decrease mortality and morbidity should be there

Recommendation for action- general:

- Develop and disseminate structured educational programme for members of the public, providers, health-care systems, and policy-makers/political leaders. Effective educational programmes should be directed to each of the important participants in an acceptable manner.
- Develop evidence-based standards for quality throughout the screening process.
- Develop and disseminate inexpensive, easy-to-use clinical management systems.
- Advocate screening through national and local venues.
- Promote colorectal cancer screening as a part of comprehensive clinical preventive care.

Recommendation for action –Programme design:

Planning the screening programme:

- A target population should identify-asymptomatic men and women, age, risk factors (e.g., familial)
- The decision to implement colorectal cancer screening should be based on the relative burden of the colorectal cancer in the population to be screened.
- The screening strategy (test, interval, age range) should be based on medical evidence (guidelines), availability of resources, level of risk, and cultural acceptance by population.

- Support by influential professional and patient advocacy groups and from the media is essential.
- Evaluate the feasibility of the proposed programme. Address the development and allocation of the resources (financial, personnel, facilities).
- Evaluate the specific cultural and language needs of the population.

Implementation of screening programme:

- Identify the target unit for implementation, and ensure communication (training and education) with providers (general practitioners and others) and the target population.
- Develop and disseminate guidelines on screening, diagnosis, treatment, and surveillance in a patient friendly and culture sensitive manner.
- Develop methods for initial patient enrollment and follow-up.

Monitoring the Screening program:

- Careful, timely monitoring of following rates: screening uptake, re-screening, and follow-up of the positive test.
- Compliance with surveillance recommendations.
- Measurement of the programme quality should be in place, and evaluated regularly.
- Outcomes, including detection rates, cancer stage distribution, adenoma detection, complications, and finally, the effect on the population incidence and mortality.

2. Colorectal cancer risk assessment tools and referral system in different countries in the world

It is believed that colorectal cancer risk varies regionally according to geographical distribution of the population. As we will see in following sections, colorectal screening is yet to be implemented fully in general population of developed countries of the world. So in different regions, colorectal cancer risk assessment tools has been introduced to identify the high risk patients needs to be screened in general population of the society. Usually these risk assessment tools are for GPs and primary care units to identify the high risk patients to be screened.

2.1. Hamilton risk assessment tool for colorectal cancer

The risk assessment tool was based on work done by Professor Willie Hamilton in the CAPER studies (Cancer Prediction in Exeter), a series of case control studies which identified symptoms of common cancers that were presented to primary care and quantified the risk of cancer associated with them. The tool acts as reminder to GPs to consider the likelihood of an individual patient aged 40 or over having lung or bowel cancer given the symptom or combination of symptoms they present with. It is presented as three tables (colorectal cancer,

lung cancer for non smokers and lung cancer for smokers) containing the risk values for each symptom in isolation or combination and is available as mouse mat or a desk easel so as to be easy to hand.

The parameter used in Hamilton risk assessment tool are: constipation, diarrhoea, rectal bleeding, loss of weight, abdominal pain, abdominal tenderness, abnormal rectal examination and haemoglobin <10g/dl.

2.2. USA National Cancer Institute (NCI USA TOOL)

A recent online tool for calculating colorectal cancer risk in men and women age 50 or older was launched, based on a new risk assessment model developed by researchers at the National Cancer Institute (NCI), part of the National Institute of Health. This new tool may help health care providers and their patients in making informed choices about when and how to screen for colorectal cancers and can be used in designing colorectal cancer screening and prevention trials.

So, by using easily obtainable information (e.g., personal and family medical history, lifestyle behaviours, and age), the tool provides an estimate of an individual`s risk of developing colorectal cancer over certain time periods (within five years, ten years, and over the course of lifetime). This risk-assessment model is first to provide an absolute risk estimate for colorectal cancer (i.e., the probability of developing colorectal cancer over a given period of time) for general non –Hispanic white population age 50 or older in United States.

In order to develop the risk assessment model, the researcher used data from two large- based case control studies. Several factors that have been previously associated with colorectal risk were shown to be predicted of a colorectal cancer diagnosis in those two studies including age; family history of colorectal cancer; consumption of vegetables; body mass index; cigarette smoking; use of aspirin or other non-steroidal anti inflammatory drugs; physical activity; use of hormone replacement therapy; previous history of sigmoidoscopy and/or colonoscopy; and history of polyps. Estimates of relative risk (comparisons of risk in one group to another) from the case-control studies were combined with population based data on colorectal cancer incidence from NCI`sSEER (Surveillance, Epidemiology and End Results) cancer registries to make the model broadly applicable in United States. [2]

"This colorectal cancer risk model should provide physicians and their patients a new tool to help in making informed decisions about cancer screening and other cancer prevention strategies. It may also assist policy makers in evaluating the usefulness of current and future population colorectal cancer screening approaches" said Andrew Freedman,Ph.D., lead author of the paper that describes the development of the risk-assessment model.

It has been observed that the majority of participants in the two case-control studies used to develop the model were non-Hispanic whites aged 50 or older, the researchers were unable to estimate relative risks for other age and racial/ethnic groups. However, there are plans to expand the tool to include these populations in the future. In addition, the tool is not applicable to individuals with certain gastrointestinal disorders (such as ulcerative

colitis or Crohn`s disease), certain inherited genetic conditions, such as familial adenomatous polyposis or hereditary nonpolyposis colorectal cancers) or a personal history of colorectal cancer. These conditions are known to carry a high risk of colorectal cancer.

2.3. Asia-Pacific Colorectal Screening (APCS) score

From a development set of 860 asymptomatic subjects undergoing screening colonoscopy, multiple logistic regression was applied to identify significant risk factors advanced colorectal neoplasia defined as invasive carcinoma or advance adenoma. Odd Ratios for significant risk factors were utilised to develop risk score ranging from 0 to 7 (Asia- pacific Colorectal Screening (APCS score). Three tiers of risk were arbitrarily defined:0-1 `average risk` (AR); 2-3 `moderate risk` (MR); 4-7 `high risk` (HR). In this study performance of the APCS score in predicting risk of advanced neoplasia was evaluated

3. Current tests for colorectal screening and emerging screening tools

The following screening methods are currently used globally:

Guaiac-Based faecal occult bleeding test (gFOBT) is at present the most frequently used method in screening programme throughout the world. It detects the peroxidase reaction of Hemoglobin, which causes the detection paper impregnated with guaiac resin to turn blue. As it can react with animal haemoglobin, dietetic restrictions are necessary to exclude the false- positive results. A number of studies showed limited sensitivity of this test for both, advanced adenomas (11%) and carcinomas (13%). With gFOBT, a decrease in mortality for colorectal cancer by 15 to 33% has been proved.

Immunological faecal occult bleeding test (iFOBT) reacts exclusively to human haemoglobin, so no dietetic restrictions are seen as necessary.Taking and assessing the stool samples are easier than the case with gFOBTs, which may explain a higher participation in the target population. A wide range of qualitative and quantitative tests are available, with varying levels of sensitivity and specificity. The advantage of quantitative tests is the possibility to set cut-off limits; the most frequently used values are 75 or 10 ng/ml. The disadvantage of iFOBT is its cost. It is, no doubt, an expensive test as compared to gFOBT. But, presently, the price is approaching that of gFOBT for qualitative tests. As this test has higher sensitivity and specificity as compared to gFOBT, iFOBT is being increasingly used in screening programmes.

New screening methods include tests which examine the stool for the presence of abnormal DNA. Generally, these tests have higher sensitivity but lower specificity than gFOBT. They are expensive tests and a major obstacle in their implementation is their price. [3]

Flexible sigmoidoscopy is an endoscopic examination with maximum reach to splenic flexure. On the basis of emerging evidence---this is a promising screening test. A number of studies are under progress to accumulate enough evidence for usage of flexible

sigmoidoscopy as a screening test based on WHO guidelines. Recommended interval varies from 3 to 5 years. A recent pilot study carried out in Darby UK* [36]. In the UK flexible sigmoidoscopy trial, 90% of all CRC detected at screening was found in the distal colon. According to one report by Sophie White et al from university of Sheffield, more than 60% adenomas are detected in left side of colon at screening age of the population and more than 70% CRC detected by flexible sigmoidoscopy at the screening age of the population.

Colonoscopy is another screening tool used in diagnostic and therapeutic endoscopic procedure which also detects lesion in proximal colon. It is more sensitive in detecting both adenomas and carcinomas. This is an established screening procedure for synchronous and metachronous tumours and surveillance of polyposis and non polyposis hereditary colorectal cancers. This is also a primary surveillance tool for multiple polyps according to guidelines. The risk of serious adverse events is higher than any other screening test with one in five hundred colonic perforation rate in expert hands. In spite of being gold standard, colonoscopy will not establish itself as an ideal population screening test due to its cost and adverse events and a lack of wide spread skills available.

Computed tomographic colonography (virtual colonoscopy) can detect lesions in the colon and rectum by reconstructing two-and three-dimentional images. To date, there is no evidence of reduction in incidence and mortality of colorectal cancer by this method in comparison with other screening tools. In cases, where caecum is not reached during colonoscopy due to patient related factors, CT colonography is the preferable screening tool to complete the examination. According to current NICE guidelines, the evidence of meta-analysis of data of 14 studies with a total of 1324 patients concluded that for CT colonography, the pooled per-patient sensitivity for polyps 10mm or larger was 88%, for polyps 6-9mm it was 84% and for polyps 5mm or smaller it was 65%. The pooled per-polyp sensitivity for polyps 10mm or larger was 81%, for polyps 6-9mm it was 62% and for polyp 5mm or smaller it was 43%. The overall specificity for the detection of polyps 10mm or larger was 95%. No significant complications were reported in the studies

Double contrast barium enema shows entire colon and rectum, although with significantly lower sensitivity and specificity than colonoscopy. The percentage of undetected carcinomas is upto 22%. This test is no longer widespread and in clinical practice due to its low sensitivity and specificity and availability of other better screening tools. Despite the fact, it still has a role in the areas in the world where colonoscopy and flexible sigmoidoscopy resources are severely limited.

It is quite obvious that Colorectal Screening is a complex process which in order to function requires the coexistence of number of factors such as a functioning invitation-reminder system, media campaigns targeted at the general public, the development of recommendations for general practitioners, patients compliance, sufficient funding, stratification of risks, and last but not least the election of the most suitable screening test. Among all available screening tests, only Fecal Occult Blood Test meets the WHO criteria.

4. Current global colorectal cancer screening pathways

4.1. Europe

Until 2007 Colorectal Cancer Screening was running or being established in 19 of 27 European countries [4] The target group contains approximately 136 million individuals suitable for colorectal screening (aged 50 to 74 years). Of this number, 43% individual come from 12 countries where colorectal population screening is performed or being prepared on either national or regional level; 34% come from the five countries where national population screening has been implemented (Finland, France, Italy, Poland and United Kingdom).

In 2007,gFOBT (which in 2003 was the only test recommended by the council of the European union) was used as the only screening method in twelve countries (Bulgaria, Czech republic, Finland, France, Hungary, Latvia, Portgal, Romania, Slovena, Spain, Sweedon, and United Kingdom). Colonoscopy was the only screening method used in Poland. In six countries, two types of the tests were used: i FOBT and flexible sigmoidoscopy in Italy, and g FOBT and colonoscopy in Austria, Cyprus, Germany, Greece, and Slovak republic. In the remaining 8 states, (Belgium, Denmark, Estonia, Ireland, Lithuania, Luxembourg, Malta, and the Netherlands), colorectal cancer screening has not been implemented yet. The age limit for target population varies across EU countries.

After 2007 Report, EU countries progressed toward the implementation of population screening programme. Recently, new EU guidelines for screening of colorectal cancers have been introduced.

In United Kingdom, a screening programme was announced in 2004 and initiated in 2006, with prospects of national coverage in 2009. It has been designed in two stages: with gFOBT tests at two yearly intervals with colonoscopy for positive tests. In 2007, the compliance was 52%. The program is carried out through regional centres falling under one of the five national hubs. The role of general practitioners is less significant here. [5]

The NHS Bowel Cancer Screening has achieved nation-wide coverage by 2010. The programme hubs operate a national call and recall system to send out FOBT kits, analyse samples and dispatch results. Consequently, each hub is responsible for coordinating the programme in their area and works up-to 20 local screening centres. The screening centres provide endoscopy services and specialist screening nurse clinics for people receiving abnormal results. Screening centres are also responsible for referring those requiring treatment to local hospital multidisciplinary team (MDT).

In Ireland, colorectal screening programme was launched in 2009 after National Screening Board Report which was published in December 2008 [6] A summary of the screening programme highlights:

- An immunochemical faecal occult blood test (iFOBT) is the primary screening tool for population-based colorectal screening programme.
- A target population for screening of all men and women aged 55 and 74 years with a screening interval of two years.

- Colonoscopy to be offered to those individuals who test positive with iFOBT

In France, Screening program was initiated in 2003, based on gFOBT tests at 2 years intervals with colonoscopy for positive result [7]. The role of general practitioners as coordinators is of crucial importance. The major advantage of French program is its good organization, with a call-recall system comprising central management at national level and individual steps taken by centres in individual departments. Asymptomatic individuals aged from 50-70yrs are mailed gFOBT tests, with the reminder at three monthly intervals for nonparticipants. Compliance in referred districts achieved 42%, and overall positive test rate was 2.7%. The screening programme has been generalised to the whole French territory since 2008.

In Italy, a nation-wide campaign was initiated in 2005; the implementation was entrusted entirely to 21 regional centres, including choice of the testing method. In Piedmont region, flexible sigmoidoscopy is the method of choice, in other regions iFOBT, with colonoscopy for positive tests. [8]

In Spain, the main obstacle to its implementation was the highly heterogeneous healthcare system, in terms of organization and insurance coverage in individual self governing units. That is why they are behind in implementation of screening program as compared to the UK, Germany, France, Italy and Finland.

In Finland, a structured screening programme was initiated in 2004. The target population, aged from 60 to 69 years (106000 individuals), was randomised into two groups. Individuals in the screening group were mailed a gFOBT test at intervals of 2 years. The finish program shows a high level compliance of the target population (70.8%), particularly for females [9]

Poland is the only state at the moment using colonoscopy as the only screening method, without the alternative of of FOBTs. An opportunistic screening programme was initiated in 2000, and by 2005, this had grown to 57 centres across Poland. The program is financed by ministry of health, independent of the overall healthcare system. The target population (Asymptomatic individuals aged 55-66 years) is recruited through general practitioners. High emphasis is placed on the quality control of the colonoscopies, with complications reported for 0.1% of the procedures, and no patient mortality. The advantage of the programme is through monitoring and evaluation, including monitoring of interval cancers. [10]

Germany was the first country to introduce a population screening program (in 1976) based on annual gFOBT for individuals more than 44 year of age. Since 2002, it has been offering participants a choice between colonoscopy at 55 year of age and FOBT at annual intervals between 50 and 55 year of age. After 55 year of age, examinations are carried out at 2 year, if the test results are positive colonoscopy is indicated. Those who undergo a screening colonoscopy with no neoplasia detected at initial examination are recommended re-examination at 10 years time if the first colonoscopy was carried out before they were 65. The positive feature of screening and data gathering is the emphasis on staging the disease at the time of its diagnosis. [11]

In the Czech Republic, CRC screening has many years of tradition. The country was the second in the world to start screening nation-wide, in 2000. In the initial years, gFOBT was offered to

asymptomatic individuals more than 50 years of age by their general practitioners at preventative medical checks, followed by colonoscopies if tests were positive. Now both gFOBT and iFOBT are being offered. The implementation of the newly designed programme is supported by intense media campaign. [12,13]

Recently, the following EU guidelines for Colorectal Screening are published:

4.2. Australia

According to a recent survey, one in 12 Australians are likely to develop the colorectal cancers in their lifetime. [14] In Australia, CRC is second most common cause of cancer-related mortality. [15] survival from colorectal cancer is stage-dependent, yet fewer than 40% of individuals are diagnosed at a localised stage. [16]

In Australia, clinical practice guidelines for the prevention, early detection and management of colorectal cancer (the national guidelines) recommend that asymptomatic people classified as "at or slightly above risk" receive FOBT screening biennially, commencing at 50 years of age, with sigmoidoscopy (preferable flexible) consider every 5 yrs. [17]. Colonoscopy screening is endorsed only for asymptomatic people who are considered to be at "moderately increased risk" or "potentially high risk"due to risk features including personal or family history of CRC, adenoma and chronic ulcerative colitis. The recently re-funded National Bowel Cancer Screening Programme (NBCSP) offers one-off Immunochemical FOBT screening to people turning 50, 55 or 65 years of age.

Implementation of biennial CRC screening in Australia for all those aged 50-74 years could prevent up to 500 deaths per year, [18] with cost effectiveness comparable to breast and cervical cancer screening Programs. [19]

4.3. United States

In USA, men and women who are 50 to 75 year old should be screened for colorectal cancer in one of the following three ways; [20]

- A high-sensitivity faecal occult blood test (FOBT) every year.
- Sigmoidoscopy every five years and a high-sensitivity FOBT every three years.
- A colonoscopy every10 year.

Colorectal screening rates rose for both men and women. The rate for women increased slightly faster, so that the rates for men and women were about the same in 2010 [58.5% for men and 50.8%for women.The colorectal cancer screening was 58.6%, below the target of 70.5%.

4.4. Asia

In Asia colorectal screening percentage is at its lowest level and research revealed that colorectal cancer burden rapidly increasing in Asian countries [21]. A study to evaluate the cost-effectiveness of FOBT, flexible sigmoidoscopy and colonoscopy in Asian countries

indicated that FOBT is cost-effective compared to flexible sigmoidoscopy or colonoscopy for colorectal screening in average risk population. [22]

The Increasing rate of colorectal cancer in Asia means that we need to take action immediately to prevent colorectal cancer and to diagnose the disease at early stages. The cost-effectiveness of screening programmes must be assessed in each individual country and research should be done to elucidate the epidemiology, genetic and environmental factors in development of colorectal cancer. [21]

5. Management of screening detected polyps

It is now widely accepted that the majority of colonic cancers arise from pre-existing adenomatous polyps (adenoma-carcinoma sequence).The supporting evidence being as follows: [23]

1. The prevalence of adenomas correlates well with that of carcinomas, average age of adenoma patients being around 5 years younger than patients with carcinomas.
2. Adenomatous tissue often accompanies cancer, and it is unusual to find small cancers with no contagious adenomatous tissue.
3. Sporadic adenomas are identical histologically to the adenomas of familial adenomatous polyposis (FAP), and this condition is unequivocal premalignant.
4. Large adenomas are more likely to display cellular atypia and genetic abnormalities than small lesions.
5. Distribution of adenomas throughout the colon is similar to that of carcinomas.
6. Adenomas are found up to one-third of all surgical specimens resected for colorectal cancers
7. The incidence of colorectal cancer has been shown to fall with long-term screening programme involving colonoscopy and polypectomy.

The patients who have undergone colonoscopy and had adenomas removed are at increased risk of developing colorectal cancer (CRC) in future, and therefore might benefit from colonoscopic surveillance. [24]

Surveillance Guidelines about colorectal adenomas are established by British Society of Gastroentrology. According to these guidelines surveillance of the colorectal adenomas depends upon ; number of polys, size of polyps and grade of dysplasia present in histology. Risk of colorectal cancer and adenomas with advanced pathology (>1cm or severely dysplastic) is greater. Risk can be stratified according to the findings at baseline and refined at each subsequent surveillance examination.

A Summary of surveillance guidelines [25] is:

- Low risk Patients with only 1-2 small <1cm) adenomas. No follow up or five yearly until one negative examination.

- Intermediate risk; Patients with 3-4 small adenomas or at least one >1cm.Three yearly colonoscopy until two consecutive negative examinations.
- High risk; Patients with >5 adenomas or > 3 adenomas at least one of which >1cm. An extra examination should be undertaken at 12 months before returning to three yearly surveillance.

The cut off age for stopping surveillance is usually 75 years but should also depends upon patients wishes and comorbidity.

Patients with incomplete examinations due to failed colonoscopies, for whatever reasons, should undergo repeat colonoscopy or alternative complete colonic examination (ct colonography). These guidelines are based on accurate detection of adenomas; otherwise risk status will be under estimated.

Large sessile adenomas removed piecemeal should be re-examined every three months. Small areas of residual polyp can be retreated endoscopically, for further check for complete eradications in three months. If extensive residual polyp is seen, open surgical resection needs to be considered. If there is complete healing of polypectomy site, then there should be sigmoidoscopy or colonoscopy at one year before returning to three yearly Surveillance. India ink tattooing aids recognition of the polypectomy site at follow up.

Stopping Surveillance.

The cut-off age for stopping surveillance is usually quoted as 75 years as the remaining life expectancy is likely to be less than the average time required for new adenomas to become malignant. After this age, it is unlikely that the benefits of surveillance will outweigh the potential risk of the procedure. However, this should not preclude further surveillance in a fit and motivated person who has a tendency to produce multiple or advanced adenomas at follow up.

The risk and benefit of adenoma surveillance needs to be balanced at all ages, particularly in patients who have significant co morbidity.

The decision to undertake each colonoscopy examination at follow up should depend not only on the number and type of adenomas, but also on the patient's age and wishes, and the presence of significant co morbidity. The Patient status should be established prior to attendance for each examination possibly by questionnaires.

6. Importance of audit in screening and screening relating colonoscopies

In any screening programme, as with any other medical service programme, adequate steps must be taken to ensure that the original objectives are being met and that methodology meets appropriate standard. The importance of maintaining the quality of screening programmes should never be under estimated. Evaluation, audit and quality control should be an integral part of any screening programme to ensure that it is achieving what it meant to be.

Colonoscopy is gold standard in important ultimate diagnostic tool in population screening programmes. Skilful colonoscopy with more then 95% caecal intubation rate is requirement for effective colorectal screening.

In the UK, before rolling out of the National Bowel Cancer Screening Programme, a large-scale study of colonoscopy practice was carried out. [26] The study demonstrated disappointing results with poor caecal intubation rates (76.95) and higher than expected complication rates. Since then there has been significant investment in endoscopic training, a quality assurance framework for endoscopic units has been implemented and National Bowel Screening Programme (NBSP) has been rolled out.

A nationwide audit of colonoscopy practice was conducted over a 2-weeks periods from 28 February 2011 until 11 March 2011. [27]. The study was performed prospectively, with the data entry occurring electronically through the purpose built website. All units performing >100 colonoscopies annually on NHS patients were included. Data on 20085 colonoscopies and 2681 colonoscopists were collected from 301units. Results showed 95.8% adjusted caecal intubation, 32.1% polyp detection rate, 92.3% resected polyps were retrieved and 90.2% o procedures achieved acceptable level of comfort. A total of 8 perforations and 52 significant haemorrhages were reported. Eight patients underwent surgery as a consequence of a complication.

The audit confirms that there has been significant improvement in performance of colonoscopy in UK since the last study reported 7 Years ago (caecal intubation rate 76.9%) and the performance is above the required national standard. But there is continuous need for assessment and audit of screening tools to keep the required national standard.

7. Colonoscopy capacity, training and accreditation

Most colon cancers are assumed to have adenomatous polyp phase. Therefore, colonoscopic detection and polypectomy provides the opportunity for cancer prevention [25]. So, colonoscopy is gold standard in high risk patients and patients with FOBT positive in population screening program. As we have discussed in previous sections, effective colorectal screening depends on available colonoscopy expertise in different part of the world

The aim of colonoscopy is to visualize whole of the colonic mucosa in order to identify pathology. A systemic review [28] of back-to-back studies has shown polyp miss rate at colonoscopy of 22% even in expert hands, especially polyps less than 1cm. Available data about polyp miss rates have shown a variation in performance between endoscopists, but this can be wider in very expert endoscopists. This shows that there is link between individual technical skill and polyps detection rate [29]. The single most important factor in the technique is withdrawal time after caecal intubation. The current recommendation is that colonoscopists should spend 6-10 minutes during withdrawal inspecting the colonic mucosa [30].

Skills in colonoscopy technique and coecal intubation rates are directly proportional to adenoma detection rate. In a standard endoscopy unit, single adenoma detection rate should

not be less than 20%. Inadequate skills in colonoscopy can also lead to higher percentage of the procedure related complications.

In 2004, the largest prospective study of colonoscopic practice in UK revealed poor outcome in terms of completion and perforation rate, as well as deficiencies in all aspect of training. The guidelines on training have been published both in UK and the USA. [30-31]

Colonoscopy training and its accreditation is a challenging task. Structured colonoscopy training is lacking in most of the countries. The NHS Bowel Cancer Screening Programme (NHS BCSP) commenced in July 2006 and recruited expert colonoscopists to carry out colonoscopies in the programme. Owing to the known variability in colonoscopy skills, strict criteria have been developed for the accreditation of screening endoscopists to minimize the risk of the complications and inaccurate and incomplete examinations.

The Joint Advisory Group of GI Endoscopy (JAG) was established under the Academy of Medical Royal Colleges and now has a number of colleges and societies with an interest in endoscopy as members who are responsible for agreeing and setting policy and strategy and advising its constituent bodies and organizations (such as GMC and NHS)on standard and in endoscopy. The Jag office manages the administrative functions of the screening Assessor Accreditation System process on behalf of the NHS BCSP which is a web-based application process.

There are several advantages of this accreditation process, to both the unit and the individual endoscopists involved. Accreditation is an essential part of preparation for the implementation of local screening programme in UK. It also provides opportunities to demonstrate high level colonoscopic skills and improve the local endoscopy service. In addition it helps clinicians who wish to teach colonoscopy locally or on courses. The accreditation process leads to the Joint Advisory Group on GI Endoscopy (JAG) certificate of competency to perform screening derived colonoscopy.

8. Hereditary risk cancer and colorectal cancer screening protocol

Inherited bowel cancer comprises of 5% of the total colorectal cancers. Based on risk of Inherited bowel cancer population can be divided into three groups: Low risk group, Moderate risk group and High risk group based on family history. Approach for screening surveillance is different in three groups:

8.1. Low risk group

It includes the individuals with:

1. No personal history of bowel cancer: no confirmed family history of bowel cancer; or
2. No first degree relative (i.e. parent sibling or child) with bowel cancer; or
3. One first degree relative with bowel cancer at or above the age of 40 years.

In this group, the risk of bowel cancer may be twice the average risk [31] and there is no evidence to support invasive surveillance in his group [24]. These individuals should be explained that they are atonly marginally increased risk of developing colorectal cancer, and that this risk is not sufficient to outweigh the disadvantages of colonoscopy. They should be educated regarding symptoms of colorectal cancer, and importance of reporting if further members of the family develop cancers. And they should be encouraged to take part in the population screening for colorectal cancer.

8.2. Moderate risk group

Individuals are included in this category if there is:

1. One first-degree relative with colorectal cancer below the age of 45 without any feature of high risk group.
2. Two first-degree relatives with bowel cancer diagnosed at any age without any of the feature of high risk group.

In this group there is three to six fold relative risk of colorectal cancer. [31]. There is only marginal benefit from invasive surveillance (colonoscopy). Current recommendations are that individuals should be offered colonoscopy at 35-40 year of age (or at presentation if they are older), and again at the age of 55 years. [24]. Coecal intubation is mandatory, as neoplasms in individuals with a strong family history are often proximal; if the caecum is not reached, virtual colonoscopy should be performed.

8.3. High risk group

In this group, hereditary non-polyposis colorectal cancer (HNPCC) and various polyposis syndromes are included. Criteria for inclusion in this group includes:

1. Family member of familial adenomatous polyposis (FAP) or other polyposis syndrome; or
2. Member of family with known lynch syndrome; or
3. Pedigree suggestive of autosomal dominantly inherited colorectal (or other lynch syndrome associated) cancers.

In this group the individuals have one upto a 1 in 2 chance of inheriting a lifetime risk and more than 50 % chances of developing colorectal cancers. They must be referred to a clinical genetics service.

According to World Gastroenterology Organisation, the low risk group and population without obvious inherited colorectal cancer history are labelled as average risk population, while moderate rick and high risk groups are considered as one group with increased risk of colorectal cancer. Global screening guidelines cascades are established in 2007 based on these risk groups.

8.4. Lynch syndrome or Hereditary Non Polyposis Colorectal Cancers (HNPCC)

Lynch syndrome is inherited as an autosomal dominant fashion. It comprises of 2% of the colorectal cancers and is commonest of inherited bowel cancers. It is associated with endometrial carcinoma (30-70%), gastric carcinoma (5-10%), ovarian carcinoma in females (5-10%), urothelial carcinoma (5%) and others (small bowel pancreas and brain)< %5

Predictive genetic testing should be offered. These individuals should have first colonoscopy at the age of 25 years or five years before earliest colonoscopy in the family and gastroscopy at the age of 50 or five years before earliest gastric cancer in family. [24]. Colonoscopy and gastroscopy should be done two yearly.

Screening for extracoloic cancers in Lynch syndrome is available. There is little evidence of benefit. Recommendation varies from centre to centre, but surveillance is advised if there is family history of particular cancer. Recommended options for extracolonic surveillance [32] are;

- Annual transvaginal ultrasound, colour flow Doppler imaging and endometrial sampling.
- Annual CA125 level and clinical examination (pelvic and abdominal).
- Upper gastrointestinal endoscopy every two years.
- Annual urinalysis /cytology.
- Annual abdominal ultrasound of renal tracts, pelvis, and pancreas.
- Annual liver function tests,CA19-9,CEA

Familial adenomatous polyposis (FAP)

It is less common than Lynch syndrome. In FAP risk of colorectal cancer is 100%.

FAP is characterised by:

- Hundred of colorectal adenomatous polyps at a young age (second or third decade of life);
- Duodenal adenomatous polyps;
- extra-intestinal manifestation;
- Mutation in the APC gene at chromosome5q

If family mutation is known, at risk family member should be offered predictive genetic testing in their early teens. If this is not possible, then clinical surveillance is required. Usually, polys develop in teenage. Colonoscopy should only be performed in symptomatic children before teenage years. Otherwise annual flexible sigmoidoscopy starting at 13-15 years of age is recommended. If no polyps are detected, 5 yearly colonoscopy at the age of 20 years with annual flexible sigmoidoscopy in the intervening years. [24]. Flexible sigmoidoscopy should be performed carefully to avoid false negative results. Chromo-endoscopy is an option in doubtful cases.

9. Future research for improvement of screening programme

Although most of the screening programme based on research has shown improved survival in patients whose tumours are detected by screening, all population screening studies are prone to biases.

Selection bias arises from the tendency of people who accept screening to be particularly health conscious and therefore atypical of population as a whole.

Length bias indicates the tendency for screening to detect a disproportionate number of cancers which are slow growing, which thereby has good prognosis.

Lead-time bias results from the time between the date detection of cancer by screening and date when it would have been diagnosed had the subject not been screened. As survival is measured from time of diagnosis, screening advances the date at which diagnosis is made, thus lengthening the survival time without necessarily altering the date of death.

Because of these biases effectiveness of any screening can be assessed only by well designed randomized trials comparing disease –specific mortality in a population offered screening with that in an identical population not offered screening.

Initially three large randomized trials, using FOBT (Minnesota, Nottingham, in Funen Denmark) [33,34,35] showed reduction in mortality. These trials provided solid ground to initiate colorectal screening programme in western countries and US.

Randomized controlled trials are expensive and difficult to manage and may be ethically questionable in situations where control group is denied treatment for the condition in question. Despite this, UK National Screening Committee will only recommend the introduction of any new programme after assessing the findings of a properly conducted randomized controlled trial. The committee also keeps all screening programmes under regular review to ensure that they continue to perform in the way intended and continue to be effective.

9.1. Bowel cancer screening programme research committee

The research committee considers the feasibility and scientific value of research projects that arises from the screening programme in UK. It encourages collaboration between researchers and tries to prevent duplication.

The committee, chaired by Professor John Scholefield, meets quarterly and has considered over 60 research applications. The area of research considered by the committee included uptake/acceptability of screening test, epidemiology/histopathology and screening technologies. Here we will mention some important research project in relation with screening.

9.2. False positive research study

A research project to investigate the causes of false positive results on Foecal Occult Blood (FOB) testing is now under way. The five year project, funded by cancer research UK is a

collaboration between university of Oxford and newly formed NHS cancer screening programmes` Research unit, which is based in the university` cancer epidemiology unit.

The pilot studies started early in 2008 and the study will eventually involve over 200,000 screening programme participants, including about 2,500people with a positive FOB test result who are categorized as normal following a colonoscopy.

9.3. UK flexible sigmoidoscopy screening trial

This trial looked at bowel cancer incidence and mortality reduction 11 years after a single screening examination with flexible sigmoidoscopy [36]

It examined the efficacy and duration of effect of ;

- A once only flexible sigmoidoscopy screen between ages 55 and 64 years.
- Removal of small polyps (<10m) during screening
- Colonoscopy only for high risk adenomas.

170,000 people were entered into the trial. Cumulative incidence, including prevalent cancers detected at screening, was reduced by 50% for the cancers in the rectum and sigmoid colon, and 33 percent for bowel cancer overall. Bowel cancer mortality was reduced by 43 percent.

The trial concluded that flexible sigmoidoscopy screening-with removal of small polyps at the examination is safe and, when offered only once between the ages 55 and 64, confers a substantial and long lasting benefit.

9.4. HTA: Frequency of follow-up for patients with intermediate grade colorectal adenomas

Beginning in September 2006, this study examined the effort of extending intervals between follow-up colonoscopies in people found to have intermediate adenomas, as defined by the British Society of Gastroentrology guidelines. It is using data from hospitals ad from bowel cancer screening initiatives to identify groups of patients with intermediate adenomas. The risk of cancer and severe adenomas will be assessed according to the interval between examinations and the number, size and features of adenomas detected.

Firstly, the study will identify whether all patients with intermediate adenomas require surveillance; secondly, whether the intervals are of the appropriate length; thirdly, it should also demonstrate how many follow-up examinations are needed. Finally, it will determine whether informing patients they need to have colonoscopy distresses them or whether they feel reassured as a result. A health economist will analyze the cost to individual patients and to the NHS and compare these with any potential benefit.

9.5. NHS bowel cancer screening programme evaluation group

The NHS Bowel Cancer Screening Programme Evaluation Group reviews and develops criteria used for evaluation and monitoring the progress of the Bowel Cancer Screening Programme.

It Includes representatives from all the professional groups in the programme as from the Cancer Screening Evaluation Unit, the Health and Social Care Information Centre and Bowel Screening Wales.

10. Current screening percentage of at risk world population and future of colorectal screening

World Gastroenterology Organization (WGO), in affiliation with International Digetive Cancer Alliance (IDCA), launched guidelines for international colorectal screening programmes after indicating the low percentage of screening programme in place in different coutries of the world. In these guidelines, they emphasise the need of some kind of screening programme in place based on locally available screening facilities

As mentioned earlier, the risk for colorectal cancers varies from country to country and even within countries. The risk also varies among individual people based on diet, lifestyle, and hereditary factors. Colorectal cancer screening is particularly challenging, as reflected in current low screening rates in most countries where there is high risk for colorectal cancer. Colorectal cancer screening is complex as there are multiple options, it requires considerable patient effort (Fecal Occult Blood Slides, Colonoscopy Preparation etc.), and it requires sedation and health-care partner for some tests (colonoscopy). [37]

It is an acknowledged fact that the lowest screening percentage of on risk population for colorectal cancer is in Asia and Africa. In most Asian and African countries, National Health Care systems and Health Insurance cover only a minority of people. So, access to healthcare facilities is limited in many rural areas and communities of low socio-economic status. In Asian countries, there is little health authority support for colorectal cancer screening and very low public awareness for this emerging epidemic in Asia. [38]

For the screening programme to be successful, multiple steps need to be taken correctly, beginning from awareness and recommendation from the primary-care physician, patient acceptance, financial coverage, risk stratification, screening test, timely diagnosis, timely treatment and appropriate follow-up. If any one of these steps is left faulty or not of high quality, the screening programme will certainly fail. (WGO)

10.1. International colorectal screening cascade

According to WGO guidelines, colorectal screening cascade consist of set of recommendations based on availability of resources in different countries of the world beginning with 1 (highest resources available) and ending with 6 (minimal resources available. [37]

10.1.1. Cascade Level 1

This is a set of recommendations for countries where high level of resources (Financial, professional, facilities) available.

For average- risk 10 yearly colonoscopies starting at 50 years.

For increased- risk patients more frequently two yearly or five yearly colonoscopies starting at 40 yrs of age.

10.1.2. Cascade Level 2

Recommendations are same as cascade level 1 but they apply when colonoscopy resources are more limited.

For average- risk once in life time colonoscopy at the age of 50.

For increased risk recommendations are same as cascade1.

10.1.3. Cascade Level 3

Recommendation are same as cascade level 1 but apply when colonoscopy resources are more limited but flexible sigmoidoscopy resources are available.

For average- risk flexible colonoscopy 5 yearly starting from 50 years of age with diagnostic workup with full colonoscopy in case of positive flexible sigmoidoscopy.

Recommendations for increased- risk are same as level 1 cascade.

10.1.4. Cascade Level 4

Recommendations are same as level 3 but they apply when flexible sigmoidoscopy and colonoscopy resources are more limited.

For average-risk screening flexible sigmoidoscopy once in life time at the age of 50 years. Diagnostic colonoscopy workup for positive flexible sigmoidoscopy or neoplasia depending on availability of resources.

Recommendations for increased risk are same as level 1 cascade.

10.1.5. Cascade level 5

Recommendations are same as resource level 4 but they apply when diagnostic colonoscopy is severely limited.

For average- risk population flexible sigmoidoscopy is recommended once in a life time at the age of 50 years. Diagnostic colonoscopy only when advanced neoplasia is detected.

Recommendations for screening increased-risk patients depend on colonoscopy resources available.

10.1.6. Cascade Level 6

Recommendations are same as for level 1 but they apply when flexible sigmoidoscopy and colonoscopy resources are severely limited.

For average -risk population, Faecal Occult Blood Testing (FOBT) should be done every year starting at the age of 50 years. The type of test used depends upon colonoscopy resources available and dietary habits of the population. The diagnostic work-up can be done either with colonoscopy, if available or barium enema, if colonoscopy is not readily available.

Therefore, recommendations for increased risk individuals are to identify them separately for special screening (level 1) and the decision depends on available colonoscopy resources. If not available, these people can be screened with average-risk individuals.

These guidelines are established considering a lack of resources in poor socioeconomically countries and can provide a base for the structured global screening programme. We hope the world will take measures to implement population screening programmes to save mankind from the cruel hands of colorectal cancer.

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